

# Non-Gonococcal Infection

## [Chlamydia - Mycoplasma]

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### History - Terminology:

- ~~H~~ Chlamydia trachomatis important agent in Both males, females - most common agent  $\rightarrow$  eliciting STDs
- First name was Chlamydozoa that was formed of 2 parts:
  - Chlamys  $\rightarrow$  = mantle or cover (covering matrix around the elementary bodies in the cells infected w/ chlamydia)
  - Zoa  $\rightarrow$  belong to protozoa.

### Pathology of Chlamydial Infection:

- The nature of chlamydia:

### Chlamydial infections:-

- Considered as bacteria b.t the following:-
  - They contain Cell wall. similar to that of Gram -ve bacteria
  - They contain Both DNA, RNA, Ribosomes metabolic enzymes
  - multiply by binary fission and they are susceptible to the antimicrobials.

### Classification:

$\rightarrow$  according to affected Host : 2 species :

- ① Chlamydia trachomatis :- Cause infection in human
- ② Chlamydia psittaci :- Cause infection in Birds.



- Those 2 species differ from each other in inclusion bodies → they produce in the infected cells and their antibiotic sensitivity:- as follows:

- Chlamydia Trachomatis produce glycogen containing inclusion bodies → so they are stained with iodine
- they are susceptible to Sulphonamides

- Chlamydia psittaci produce inclusion bodies that contain no iodine, and they are
- No sensitive to sulphonamides

→ according to the affected system:- 15 serotypes  
3 groups

① Serotypes A, B, B<sub>1</sub>, C

- Responsible for The Hyperendemic Trachoma of The eye

② Serotype D-K

- Responsible for The Mucosal Surface of genital tract
- Relatively non invasive

③ Serotypes L<sub>1</sub>, L<sub>2</sub>, L<sub>3</sub>

- Responsible for the Lymphatic tissue infection of the genital tract → lymphogranuloma venereum
- Relatively invasive

## ④ pathogenicity and growth Cycle in the Host cell

- The organism passes by 2 Phases before and after invasion of the host cells as:-

① Extra Cellular phase:  
(elementary body)

- infective phase
- start by attachment to the Host cell followed by its phagocytosis by the host cell.
- its Not Digested and undergo organization to the 2nd phase or the initial body.

- These 2 factors of enhanced phagocytosis and inhibited Digestion are → important Virulence factors



## ② Intracellular phase (Initial body) (Reticular body)

- This body uses the host cell molecules to produce chlamydial nucleic acids and proteins → Divides by Binary fission followed by 2nd organization to form the elementary bodies

- Finally → the host cell Rupture → with Release of these elementary bodies to infect other host cells

- The whole cycle takes 48-72 hr

## ★ Clinical picture of chlamydial inf

↳ Serotypes D-K → produce mucosal affection, mainly similar to gonorrhoea with some Difference That will be stressed upon mainly non-gonococcal urethritis and Reiter's Syndrome

- Serotypes L1, L2, L3 → produce Lymphatic affection and lymphogranuloma venereum

## ⊕ Difference Between Gonococcal, Non-gonococcal Urethritis

↳ non gonococcal • Long incubation period. That may Range from 1 week to 5 week or longer

• may be Asymptomatic or with Scanty urethral Discharge that may be Thick and purulent

• Finally :- there may be no symptoms apart from urethral itching

## ⊕ Reiter's Syndrome :-

• Triad of :- ① Urethritis ② Conjunctivitis ③ Arthritis  
↳ may be other mucocutaneous manifestations That vary from one to other.

• it's an episode of arthropathy occurring within 1 month of an episode of Urethritis or Cervicitis



## → Other less Common names of RS

- Sexually acquired reactive arthritis SARA
- Conjunctivo-urethral-synovial syndrome
- Venereal arthritis
- arthritis urethetica.
- Idiopathic blemorrhoeal arthritis

## → Etiology of Reiter's

- unknown, may involve one or more of the following factors:-

### [1] Genetic Factors:

60-70% of pts w RS → +ve histocompatibility antigen HLA-B27

### [2] Infective Factors:

- 1-4% of cases with non-gonococcal urethritis may followed by (RS) NGU
- It may occur also after gonococcal infection

⊕ RS following NGU → is totally different from arthritis that occur as a result of disseminated gonococcal infection D.t gonococcal urethritis (GU)

⊗ The Arthritis in RS is D.t abnormal immune Response to NGU

⊕ The Arthritis Gonococcal is Due to actual (48)  
Dissemination of gonococci from Urethra to Joints.

### [3] Immunological Factors:

- most of pt's w RS - High antichlamydial antibody titres.

## → Clinical picture of Reiter's

### [1] Mucocutaneous Manifestations:

- Urethritis precedes the appearance of RS

#### • Mucocutaneous lesion:-

- ↳ Painless erosive Dermatitis
- ↳ small ulcers on the glans penis in males or the vulva in females leading to formation of Circinate balanitis, Circinate Vulvitis.

- ↳ Small erosions and ulcers on the tongue or oral mucosa.

#### • Cutaneous lesion:

- ↳ Scaly erythematous psoriasiform patches mainly on palms-soles [keratoderma blemorrhagica]



## ② Articular manifestations :

- mainly : Arthritis
- (non-suppurative, occur within 1 months of urethritis)
- First joint affected is Sacroiliac joint leading to → Sacroileitis
- The Knee joints :-
  - ↳ pain ↳ Tenderness ↳ effusion
- The small joints of fingers :-
  - ↳ Fusiform Dactylitis
  - ↳ Tenosynovitis
  - ↳ Sausage Digits

## ③ Ocular Manifestations :

- mainly : Conjunctivitis
- Rarely : - iritis, uveitis

## ④ Other Rare manifestations :

- CVS :- - Carditis
- aortitis & thrombosis

- Neuro :- meningitis, encephalitis, neuritis<sup>49</sup>
- Systemic :- generalized lymphadenopathy  
thrombophlebitis  
Amyloidosis

- The Cause of Death: D.t aortitis, Amyloidosis

## → Laboratory investigations

- No specific Lab test For RS.
- Lab finding :-
  - ↳ ↑↑ ESR, CRP, Circulating immune complex, Leukocytes.
- The synovial fluid of affected joints :-
  - ↳ Turbid
- Culture of fluid → -ve (sterile)
- it shows → specific Cellular Response to the antigens of the genital or enteric microbes

## → Treatment

- 1 - Antibiotics → according to culture and sensitivity
- ↳ The possible infections



## 2 - NSAIDs →

- Very effective in ttt of Arthritis  
such as:- Indomethacin 50 mg/3 times daily.  
Oral steroid → not much effective

## 3 - Cytotoxic Drugs → (Methotrexate)

4 - Immunosuppressive Drugs → (Azathioprine)  
effective in severe cases.

## ★ Laboratory Diagnosis of Chlamydial inf

### [A] Culture Techniques:

- 1- Specimen → obtained by scrapping of Urethra or Cervix by swabs to obtain epithelial cells
- 2- The chlamydia is obligate intracellular organisms so they are found in the scrapped material rather than the Discharge or Urine
- 3- The obtained specimens are → refrigerated and transported to the Laboratory within 2 hrs in a transport medium that contain:- Sucrose and antibiotics to

inhibit other organisms

4- Then inoculated into Tissue Culture Cell monolayers that are treated by:- irradiation or antimetabolites → to inhibit Cell Division in those tissue Culture.

5- This induces the formation of giant cells that allows the growth of chlamydia inside their abundant cytoplasm

6- Example of those tissue cultures:-  
- McCoy Cells treated with Cycloheximide.

7- After 48hr → The Culture is examined after Staining with Iodine stain, Giemsa's stain or immunofluorescence stain to Detect intracellular chlamydia Inclusion bodies.



## 8 - Disadvantages of the culture

- Sure Diagnostic Tests
- Indicated before therapy to detect antibiotic sensitivity of the organism and after therapy as a test of cure

## B Non-Culture Techniques:-

### 1. Gene Detection:-

- PCR - LCR techniques.

#### - advantages:

↳ not invasive as the specimen is the Urine sample

↳ sensitive and specific

↳ very good Screening Tests specially in asymptomatic pts

### 2. Antigen Detection:-

#### • ELISA:-

- depends on detection of chlamydia antigen in the sample by adsorbing

it to polystyrene beads coupled to chlamydia monoclonal antibodies.

- This adsorption is detected in Spectrophotometer.

- This Test named as Chlamydiazyme.

- has good correlation with the Result of the Culture.

- more available, Less expensive

#### • Immunofluorescence test (MicroTrak test):-

- Detect:- Chlamydia antigen by use of specific monoclonal antibodies to chlamydia conjugated with Fluorescein

- The advantages of Both Tests that they are sensitive and specific for screening But

- The Disadvantages are that they are Not recommended as test of cure because the antigens may persist despite killing of organism

### 3. Antibodies detection:-

- The Serological tests → Done by Micro-Immuno Fluorescence OR Complement Fixation. to detect antichlamydial antibodies.



## ★ Treatment of chlamydial inf.

### [A] Difficulties in treating chlamydia as compared to Gonococci:-

#### 1- Compliance of the pt:-

- treated effectively by a single Dose whereas chlamydia usually needs multiple Doses a factor that ~~to~~ the pt's Compliance.

#### 2- Cure rate:-

- may reach up to 95% → for gonococcal infections
- 80% → in non-gonococcal infection

#### 3- Culture:-

- The Culture of chlamydia are expensive
- Time Consuming
- Not always available.
- They are the only sure test-of-cure

### [B] Treatment Recommendations:-

#### ★ First choice regimens:-

- Azithromycin 1gm single Dose orally
- Doxycycline 100 mg orally Twice daily for at least 7 days
- Tetracycline hydrochloride 500 mg orally 4 Times daily for 7 days.

#### ★ Alternative Regimens:- [if others are contraindicated or intolerated]

- Erythromycin 500 mg orally 4 times daily / 7 days
- Ofloxacin 400 mg orally twice daily / 7 days
- Erythromycin → safe in pregnant women

### [C] Treatment Details:-

#### 1- Azithromycin:-

- azalide macrolide antibiotic
- used as a single (1gm) Dose orally or divided into 500 mg in the first day 500 mg in the 2nd day.
- High cure rate for Both → gonorrhoea
- S/E → gastric Troubles → chlamydia



## 2 - Tetracyclines :-

- active against chlamydia
- Not giving with milk or milk products that inhibit their activity
- Contraindicated → pregnancy - children
- Some strains of chlamydia show partial resistance to this group.

## 3 - Macrolides :-

- Erythromycin → effective as tetracycline against chlamydia
  - inactive against Mycoplasma hominis.
- safe in pregnancy

## 4 - Quinolones :-

- The best of this group is: Ofloxacin

## 5 - Other Antibiotics :-

- \* The following antibiotics Not indicated for the of chlamydial infections: Due to:

## - Penicillins groups :-

↳ effective against chlamydia in vitro only  
But clinically the effective Dose should exceed 30 million units of penicillin/per day  
So they are not used

## - Rifampicin :-

↳ effective against chlamydia in vitro  
But clinically there is Rapid development of resistance to it. → So not used.

## - Aminoglycosides - Cephalosporins.

↳ ineffective against chlamydia.



# 2 Mycoplasma infections :-

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## ★ 3 main groups :-

- ↳ Ureaplasma Urealyticum
- ↳ Mycoplasma hominis
- ↳ Mycoplasma genitalium

## ★ They are :-

- normal inhabitants of the urogenital tract in
  - ↳ males
  - ↳ females
- may have pathogenic Role in Urogenital infections

## ★ Clinical manifestations:

### [A] manifestations in the Males :-

#### 1- Urethritis :-

- Some Cases of non-gonococcal Urethritis are Caused by : Mycoplasma hominis + Ureaplasma Urealyticum

## 2- Epididymitis :-

- evidence That some Cases of epididymitis are Caused by : Ureaplasma , Proved by : epididymal aspiration

### [B] manifestations in the Females :-

#### Bacterial Vaginosis

- offensive homogenous non-pruritic grey discharge
- absence of inflammatory changes in the vaginal wall.

#### Pelvic inflammatory Disease

- Caused by :- Ureaplasma Urealyticum

and Mycoplasma hominis

That's way bacterial Vaginosis's Replace "non specific vaginitis"

### [C] manifestations in male & Females :-

- Mycoplasmal infections in Both sex → may followed by Reiter's Syndrome



## Clinical manifestations in Infants:-

- Pneumonia • Fever • RDS

## Laboratory Diagnosis

### ① Culture:-

- Not Recommended as a routine test
- The Diagnosis Depends mainly on Clinical picture
- The main indications for Culture → in cases of persistent non-gonococcal urethritis that are -ve for chlamydia in order to do antimicrobial sensitivity Test to Direct the Therapy

### ② The Swabs → streaked into mycoplasma/ureaplasma selective medium

- Contain  
agar base  
yeast horse serum  
manganese sulphate  
urea, ampicillin

- They are incubated anaerobically for 55 48hr at 37°C.

- Mycoplasma produces large colonies (50-500 mm in Diameter) with the ch.ch:- fried egg appearance

- Ureaplasma → produces tiny colonies (50-100 mm) with the ch.ch Brown colour D.t → its ability to Utilize Urea

## Treatment:

### 1. Tetracyclines:

- effective against Both  $\left\{ \begin{array}{l} \text{Chlamydia} \\ \text{mycoplasma} \end{array} \right.$
- Some Resistant strains of ureaplasma → Reported
- This Resistance Caused by :- The same plasmid that Codes for resistance of the gonococci to tetracycline

### 2. Erythromycin:

- alternative to tetracycline in Cases of :-  
↳ Resistance      ↳ pregnancy

60 - The Dose = chlamydia



# Lymphogranuloma Venerum

## ★ Terminology :

- Systemic Disease Caused by Sexual Contact
- Affect mainly the lymphatic system
- Caused by → chlamydia Trachomatis Serotypes (L1, L2, L3) that have Tendency for invasive lymphatic infection
- Other name → Esthiomene → means Decay or Destruction occur in Vulva in late stages.
- Other rare names :-
  - ↳ Tropical bubo, Frei's Disease, fourth venereal Disease, Nicolas-Fave Lymphogranuloma inguinale.

The transient, painless nature and the hidden site of the Ulcer in females (post-vag. wall) → Cause late complications

## ★ Clinical picture :

### (A) Primary Stage :-

- after IP (1 week - 4 weeks) → There may be a small ulcer → That may be on the Coronal Sulcus or intra-Urethral → in males
- Urethral Discharge, post-wall of vagina or Cervix → in female

→ Occur in :- Rectum in 
 ↗ Females  
 ↘ homosexual males

↳ proctitis, tenesmus, Discharge, Bleeding from Rectum.

↳ The Ulcer → small, transient, associated w/ Lymphangitis, Swelling of genital organs

↳ Heal → Spontaneously



## B Secondary stage:-

- Start (1 wk - 4 wks) after Disappearance of the Primary Lesion
- Include The Following:-

### Inguinal manif

- painful tender enlargement of inguinal L.N on one or Both sides → **inguinal bubos**
- The enlarged inguinal L.N formed **2 groups** of swelling above, and, Below the inguinal ligament → that forms groove Between the 2 groups of swelling → **groove's sign**
- Finally → L.N fluctuate → Discharge of yellow purulent material with **ulceration** of overlying skin

### Systemic manif

- ↳ Fever
- ↳ headache
- ↳ Arthralgia
- ↳ in sever neglected Cases:
  - ↳ encephalitis
  - ↳ meningitis
  - ↳ hepatitis
  - ↳ Skin Rash:-
    - Erythema Nodosum
    - Erythema multiforme

## C Tertiary Stage:-

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### Anorectal manif

- prolonged Lymphatic Obstructions and granulomatous invol of rectal-mucosa
- ↓
- end in Rectal Stricture & perirectal fistulae in females and homosexual males

- Occur in ptns e- HIV infection Due to → Reactivation of the Disease

### Genital manif

- prolonged Lymphatic Obstruction → give rise to → genital Elephantiasis with → excessive Destruction of the genital organs → Esthiomene in females Saxophone in males
- There may be elephantiasis in Lower limbs



## ★ Causes of Death in lymphogranuloma venereum

1 - neglected late cases (main cause)  
include → gut perforation with peritonitis  
Due to :- anorectal strictures  
OR Destruction of its wall.

2 - Carcinoma → may Develop on top of long standing cases of genital elephantiasis OR rectal fistula and stricture.

## ★ Lab Diagnosis :- ch. 5

## ★ Treatment: [A] Recommendations:-

### [1] First choice Regimens:

- Tetracycline hydrochloride 500 mg orally 4 Times Daily for 14 days
- Doxycycline 100 mg orally twice Daily for 14 Days

## ② Alternative Regimens:

(if Tetracycline are poorly tolerated.)

- Erythromycin 500 mg orally 4 times Daily for 14 Days
- Sulphamethoxazole 1 gm orally twice Daily for 14 Days

## [B] Treatment Details:-

→ Fluctuating inguinal lymph nodes → Aspirated by the use of a wide pore needle inserted into a healthy area of skin away from the L.N.

→ if they are incised and Drained There will be prolonged Discharge

→ • Delayed healing  
→ perirectal, rectovaginal fistula and strictures → should Surgically Corrected

→ Suspicious areas → should excised

[63] and subjected to pathological examination to exclude → Carcinoma in Long standing cases



# Granuloma Inguinale

## ★ Terminology :

- Chronic Destructive Disease of the genital organs and adjacent areas
- it was known in the past **Donovanosis**
- The causative organism

**Calymmato-  
Bacterium  
granulomatosis**

→ The granulomatous ulcer → Spreads in a serpiginous manner to the adjacent inguinal folds → to form indurated inguinal masses = **pseudobubos**  
that's because → The inguinal L.N not enlarged  
So there is No actual bubos

→ Scarring occurs in → chronic Cases with excessive formation of mutilating fibrous tissue that may spread along large areas of the genital organs, inguinal regions, the lower abdomen, thigh → forming extensive granuloma encuirasse

## ★ Clinical picture :-

### (A) manifestations of G. Inguinale :

- after IP (9-90 Days) the primary lesions :-
  - painless pepule OR nodule on genital organs in Both males & females
- The lesion Rapidly produce → Ulcer with granulomatous Base, rolled edges

### (B) Complications :-

- 2ry bacterial infection → in neglected Cases with fusiform bacilli →



Formation of Large painful Foul smelling  
Destructive (phagedenic) Ulcers on the  
genitalia with stenosis of the Urethral,  
vaginal, anal orifices.

- The chronic ulcerative granuloma of  
the external genitalia (that characterizes the  
granuloma inguinale and other Tropical Diseases)  
↳ maybe Risk Factors for spread of  
HIV infection
- Finally D.t. → the prolonged Ulceration  
↳ 2ry infection  
↳ Irritation  
↳ Sq. Cell Carcinoma on  
Top of long standing Cases

## ★ Laboratory Diagnosis:-

### ↔ Introduction:-

- Causative organism:- Calymmatobacterium  
granulomatis  
↳ gram -ve bacillus → Can't cultured

on artificial media.

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• So the main method of Diagnosis  
depends upon

↳ Demonstration of organism in  
The scraping

↳ Biopsy from lesion.

• Biopsy from lesion is important →  
To exclude Carcinoma → in Long-  
standing Cases.

• The Diagnosis has 2 aims:

↳ Demonstration of the organism  
↳ Exclusion of Carcinoma.

## (A) Demonstration of Organism

### ★ Technique:-

- Scraping from the lesion  
- Better → small piece from the edge  
of the lesion → Crushed and.

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spread Between 2 slides

- The Resultant from smear is → air-dried heat fixed, stained with Giemsa stain eosin stain, thiazin, wright stain

### ☀ the organism :-

- Calymmatobacterium granulomatis is → gram -ve → non sporing Capulated Bacillus
- Seen: Inside intracytoplasmic vacuoles of the histiocytes OR polymorph nuclear leukocytes.
- multiplies by: Binary Fission till production of about 20 organisms inside the vacuole.
- The organism stain :- Blue, Black with wright stain → appear to have bipolar staining as its 2 poles → giving it a (safety-pin) appearance.
- The capsules stains :- pink around it



## 61 (B) Exclusion of Carcinoma:-

- Histology show:-

- wide spread acanthosis
- Dermal infiltrations with plasma cells and histiocytes, few polymorphs with the organism inside their vacuoles.
- the edge → epithelial proliferation that should be differentiated from malignant change

### ★ Treatment:-

#### ① Conventional therapy:-

α. Tetracycline hydrochloride 500 mg 4 times daily for 3 weeks

α. Sulphamethoxazole - Trimethoprim Formed & 800 mg & 160 mg respectively

#### ② Recent therapy:-

- Norfloxacin - Azithromycin

- INH → G. inguinale → fail to Response.



# Chancroid

## ★ Terminology :-

- STDs → ch. ch By genital Ulceration
- in past → was considered the same as Syphilitic chancre.
- But it's a Distinct Disease Caused by Gram -ve bacillus "Haemophilus Ducreyi"
- Other names: Soft, sore, soft chancre  
↳ Ulcus molle

③ Tropical STDs :  
 ↳ lymphogranuloma venereum  
 ↳ granuloma inguinale  
 ↳ Chancroid

⑤ Classic STDs  
 ↳ The 3 tropicals  
 ↳ Syphilis  
 ↳ gonorrhoea.

## ★ Clinical picture :-

### ① Manifestations :-

#### 1- Chancroid ulcer :-

- after IP (1 week - 3 weeks) (usually < 1wk)
- ↳ The ulcer begins as a transient papule that rapidly breaks into a painful ulcer :- with the following ch. ch :

#### • Inspection :

- ↳ number : single, multiple
- kissing ulcers on 2 opposing surfaces on the under surface of the prepuce and glans penis

#### ↳ Site :

- mucous surface of prepuce
- Coronal sulcus
- Urethra in the males
- The frenulum

67 - labia majora, the Fourchette, clitoris  
 the Urethra in Females



- ↳ Size: 2mm to 2cm
- ↳ Shape: Irregular or Serpiginous
- ↳ Edge: Undetermined
- ↳ Floor: (seen Not felt)  
Covered w<sup>th</sup> granulation tissue or purulent exudate

### • palpation:

- ↳ Tenderness: - ptn feel pain on Pressure on the lesion. Ulcer tender
- ↳ Base:  
examiner puts his thumb and index finger around the edge of the Ulcer and try to approximate them.  
- The Ulcer is soft

### ↳ Fixation:

examiner puts his thumb and index finger around the edges of the Ulcer and tries to move the whole ulcer over the underlying tissue.

- The ulcer is Not fixed

(Can be moved over the tissue)

## 2- Genital Discharge:

- purulent Urethral Discharge occur in cases with intraUrethral lesions
- Chancroid has to be differentiated from other causes of genital ulcers as well as other cause of genital Discharge

## 3- Regional L.N:

### • Inspection:

- ↳ Number: - multiple
- ↳ Site: - Inguinal group of L.N
- ↳ Side: - Unilateral in 50% of ptns
- ↳ Size: - Large size
- ↳ Shape: - Irregular masses (chubbs) D<sup>t</sup> periadenitis
- ↳ Surface:  
overlying skin may be Red or Break with Suppuration after (1-2) weeks and formation of Sinuses

### • palpation:

- ↳ Tenderness: Very Tender
- ↳ Consistency: The L.N are either soft or show Fluctuation when pus is formed
- Fluctuation is wave-like motion produced by palpation
- Body swelling when it contains fluid



↳ Fixation:- L.N fixed to each other as well as overlying skin.

## (B) Complications:-

- Stenosis of the prepuce (phimosis)
- Difficulty in its retraction (paraphimosis)
- 2ry Bacterial infection with fusiform bacilli → Destructive phagedenic ulceration that led in the past to
  - Destruction of the glans penis
  - gangrene
  - urethral stricture
- The genital ulceration in Chancroid →  
↑ The spread of HIV infection specially in Africa.

## ★ Laboratory Diagnosis :-

### • Introduction:

- The causative organism is *H. ducreyi*
- Gram -ve bacillus that needs to be cultured on Blood enriched media.

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- The Diagnosis depends on:-

- Demonstration of the organism mainly use → Blood Culture (rather than smear that is not reliable)

- The Diagnosis has 2 aims:-

- ↳ Demonstration of organism
- ↳ exclusion of other causes of genital ulcers

## [A] Demonstration of the Organism:-

### • The techniques:

- Tissue taken from the edge of the ulcer or from aspiration of the bubos
- 1- Smear stained with Giemsa stain, wright stain, Gram stain
- 2- The Culture is more reliable.
  - it's grown on Blood-enriched Gonococcal agar Base OR Mueller-Hinton agar Base
  - Culture media → incubated at 33°C in environment with 100% humidity and CO<sub>2</sub>.



- within 48 hrs → The Colonies appear as yellow-gray Dome Shaped 1 mm in Diameter → adhesive when touched with a wire.

3 - Recently → Chaneroid Can Diagnosed By PCR (more sensitive & more specific)

### ● The Organism:-

- small gram -ve Bacilli with Rounded ends
- appear in groups or rows Containing about 20 organisms giving appearance [school of fish or railroad tracks]

### ● Histopathology:-

- The Biopsy show:- 3 distinctive Zones
- 1- patchy necrosis of the epidermis with occasional acanthosis and Neutrophils in the superficial Zone
- 2- proliferation of the Endothelium

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of The Blood vessels in mid Zone  
3- plasma cells and lymphocytes infiltration in the Deep Zone

### [B] Exclusion of other Causes of Genital Ulcers

- Differentiated from other Causes of genital ulcerations Including:

- \* Chancre : by darkground microscopy
- \* Granuloma Inguinale : has some similarity
- \* Herpes progenitalis

### (★) Treatment:-

#### ● Introduction:-

- liable to produce antibiotic resistance.
- This resistance is an extra-chromosomal or plasmid mediated.

↳ Those plasmids are similar to the plasmids of N. gonorrhoea.



- They can mediate Resistance against:
- Ampicillin - tetracycline - Sulphonamides
  - Trimethoprim

→ So ∴ proper antibiotic Sensitivity Testing.

∴ adequate Att

∴ prolonged follow up

is essential → to ensure the Cure.

→ Being one of the Ulcerative STDs ∴

most important to test for HIV

at the initial visit and after 3 months.

### Single Dose Regimen

- Azithromycin 1gm orally
- Ceftriaxone 250mg I.M

### Multiple Dose Regimen

- Erythromycin 500 mg orally / 4 times / for 1 wk
- Ciprofloxacin 500 mg orally / twice / for 3 days
- Amoxicillin 500 mg combined w/ Clavulanic acid 125 mg orally / 4 times / 3 days

⊛ The enlarged fluctuating inguinal L.N (bubos) → should never be incised

↳ as the healing is very Slow

⊛ They should be Aspirated by a wide bore needle through healthy area of skin away from the bubos



# Syphilis

## ★ Terminology - History :- Future:

- D.F :- prenatal or acquired systemic infection.
- organism :- Treponema pallidum
- site :- occur at any tissue or vascular organ
- Names :- many names and many victims :-

→ Christopher Columbus

→ who accidentally acquired the Disease and transmitted it on his Return to Europe to start the epidemic of this New Disease in Europe.

The king and queen of Spain:

→ Received him at that time with the highest honours for his Discovery of the new world.

Surgeon John Hunter:

→ acquired the Disease by self-inoculation of venereal Discharge of a ptn → unfortunately this ptn had syphilis and gonorrhoea at the same time who at past considered one disease.

- All Deaths Due to Syphilitic Heart Disease.

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• Other names :- Lues = pestilence or plague (which given to any contagious malignant epidemic D)

great pox :- as opposed to small pox which was considered at that time relatively mild epidemic

great imitator :-

• Sir William Osler says :-

"known syphilis in all its manifestations and relations and all other things clinical will be added into it"

• The primary lesion of syphilis "Chancre" means in latin "Cancer"

→ The actual link Between syphilis and Cancer → leukoplakia of the tongue → occur interitery stage → predispose to Carcinoma of tongue

• Future :-

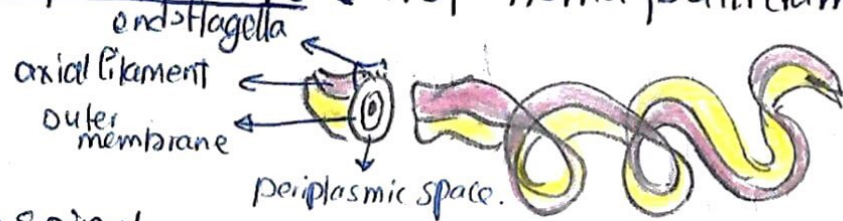
→ after availability of Penicillin therapy → the false sense of security from syphilis

→ The situation changed Dramatically with appearance of HIV inf. the new plague of 20th Century



## ④ Causative Organism:-

### • Spirochaete (*Treponema pallidum*)



→ Spinal organism of (6-12) regular coils with length of (6-12  $\mu$ m) width (0.12-0.25  $\mu$ m)

→ show 2 Types of motility :-

1. Locomotion :- informal Corkscrew or propulsive movements
2. Change in shape in the form of :- angulation, elongation undulation

→ The tiny size of the organism renders it below the level of resolution of conventional light microscopy and hence the Darkground microscope → should be used to observe it and its motility directly.

→ It can be stained by silver or immunofluorescence stains though they are not used practically.

### • Other Spirochaetes :-

- *Borrelia refringens* • *B. balanitidis* should be differentiated from *T. pallidum*
- *Treponema* that cause pinta, yaws (*T. Caraleum*, *T. pertenue*)
- *T. microdentum* or *T. macrodentum* that are responsible for Dental Caries found in oral cavity
- non-pathological Rieter strain
- Nicol pathological strains

## ④ Pathology:-

### (A) Early phase :-

- Organism enter the body through abrasion in skin or M.M → Local tissue Reaction of two 2 components:

1. Cellular infiltration with plasma cells and lymphocytes
2. Vascular reaction :- Endarteritis



obliterans (Thick, Hypertrophic intima)

- The organism Reach the Regional L.Ns leading to → Lymphadenopathy followed by → invasion of Blood stream.

### B<sup>3</sup> Late phase :-

- There is Balanced state Between Trepanoma that give No symptoms and antibodies in the Serum
- If this balance is Disturbed → Late manifestations occur → in form of gumma show:- the same tissue Reaction
  - + - Necrosis
  - Vascular or neurological affection.

## ★ Classification:

(A) Acquired Syphilis : Divided acc. to time

● Early phase:

- During the first 2 yrs

- The ptn is infective to others.

- It includes :-

↓  
Primary stage

- One month
- Occur after incubation period of 9-90 days

↓  
2ry stage

- Two months
- manifested by:- Generalized affection
- Both stages:- Asymptomatic

● manifested by:-  
Chancere

- Early Latent Syphilis

↳ means that the ptn is still within the first 2 years of infection

↳ because the ptn is Asymptomatic.

● Late phase :-

- Occur after the first 2 yrs of infection.

- The ptn is Not infective to others

- It includes :-

↳ ptn is Asymptomatic  
↳ Late Latent Syphilis :-

↳ ptn has passed the first 2 yrs of infection



## ↳ Tertiary stage:-

- This stage after 3 or more yrs +
- main manifestation is **Gumma**.

## ↳ Quaternary Stage:-

- occur after 20 or more years
- the main manifestations are **CVS** and neurosyphilis
- Both stage are **Asymptomatic**.

## (B) Congenital Syphilis:-

Early phase	Late phase	Stigmata (Remainders)
→ occur within first 2 yrs	→ occur after the first 2 yrs	- The permanent scar of early lesions
- Infective	- Not infective	

# Primary Syphilis

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• after 1P (9-90 days) → the Chancere appears.

start by papule that gives painless ulcer  
with the following Criteria:

## (A) Inspection:-

↳ number: Single → D.t local immunity

↳ Site:

- Genital → male → Coronal sulcus  
→ glans penis  
→ Frenulum  
(concealed) inside urethra  
→ meatus

Female → labia majora, labia minora  
→ meatus, Cervix (concealed)

Extragenital → Anus, lips, tongue, nipple, areola.

↳ Size: (0.5-2cm) in Diameter

↳ Shape: Rounded or oval

↳ Edge: Raised at periphery, slopping toward center

↳ Floor: (seen not felt) → clean, pale or red  
→ oozing serous fluid



## ② Palpation:-

↳ Base:- (felt not seen)

- Indurated :- if the lesion is held between index and thumb,
- They can't be approximated

↳ Tenderness:- Abscent

↳ Fixity:- not fixed to deeper structures (if the lesion is held between index and thumb → it can be moved)

↳ Fate:-

- Show healing without treatment in about 2 months with a thin scar

## ★ Variants of primary Syphilis:-

### 1. Chancre Redux:-

chancre Develops on the scar of previously healed chancre.

2. The chancre Painless - Not Tender :- Due to Degeneration

of nerve axons in the lesion

- it may be painful → if there is 2ry infection that is common in AIDs pts

3. ptne 1ry Syphilis who present Neither Chancre nor inguinal L.N:-

- occur in female & Chancre on the Cervix → so no lesions on the genitalia

- also :- the Cervix Drains to the deep iliac L.Ns  
So no inguinal nodes

### 4. pseudochancere Redux:-

• It's a Gumma → Develops on the Scar or healed chancre (Not treponema or L.N)

## ★ Inguinal L.Ns:-

- Bilateral - Symmetrical - Painless Enlargement
- Rubbery in Consistency - Freely mobile
- Not Tender - the overlying skin → Normal
- Some ptne may present by :- enlarged L.N with healed or abscent chancre (Bubon d'emblee)



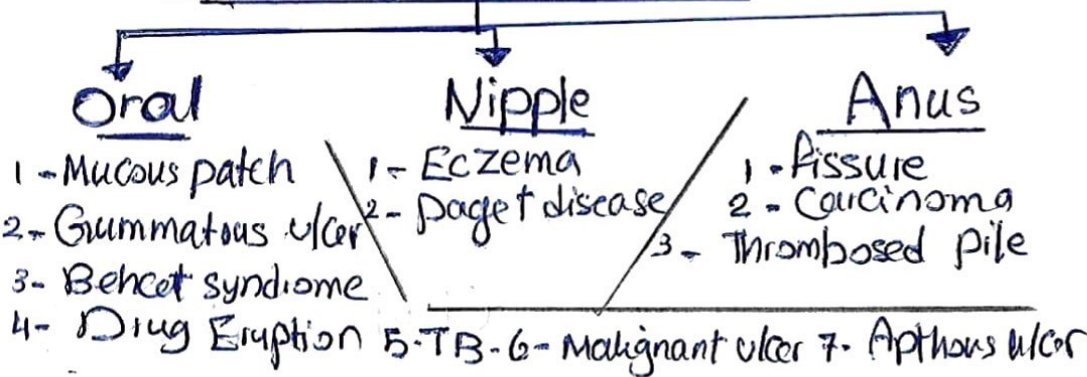
# ★ Differential Diagnosis :-

## [A] Genital Chancre :-



- |                              |   |
|------------------------------|---|
| 1. Traumatic Ulcer (Scabies) | 1. Herpes progenitalis  |
| 2. T.B Ulcer                 | 2. Chancroid  |
| 3. Herpes Zoster             | 3. Lymphogranuloma venereum   |
| 4. Malignant ulcer           | 4. Granuloma Inguinale  |
| 5. Ulcer of Drug Eruption    | 5. Scabies  |
| 6. Bilharzial ulcer          | 6. Primary HIV Ulcers   |
| 7. Behcet syndrome           | 7. Mucous patch ulceration of 2ry syphilis<br>gummatous ulcers of Tertiary Syphilis |

## [B] Extragenital Chancre.



# ★ Diagnosis of 1ry syphilis <sup>72</sup>

## [A] Darkground Microscopy

- The only Sure method for Diagnosis
- The idea :-
  - Depends on the Observation of the organism and its motility by making light rays diverge from the looking eye → Dark Background.

When these Divergent rays face the organism → they deflected towards the eye.

- So the Organism appears Luminescent against Dark background and its motility can be examined.

(Done by → change the diameter of the opening of the condenser to diameter of

## ★ the material for examin (0.8 cm)

- From the ulcer or L.N

## ★ Exudate from the ulcer :-

The ulcer should be cleaned with gauze soaked in water OR Saline to remove Scabs. (not antiseptic → kill the organism)



- This is important → to Remove Saprophytic organisms in Dirty genital lesions as :-  
[*Borrelia refringens*] [*B. balanitidis*]
- Sulphonamides given in a dose of 1 gm / 4 times / Day are useful to guard against Sepsis
- They have the advantage of being non-treponemoidal Drugs.

✱ Aspirate from L.N :- indicated in Cases with -ve results on ulcer exudate or there was antiseptic application on it or if it is hidden or healed.

(B) Serological Tests :-  
+ve Results in 50% of ptns.

## Secondary Syphilis

✱ General manifestations :-

- after period of about 8 weeks from the appearance of chancre,

78

50% of untreated ptns → Presented by :- 73

- Severe headache
- Fever
- meningism

Due to early invasion of CNS

- for the same reason → There may be Nerve Deafness

- Eyes :-

→ Iritis → Choroidoretinitis

- Scalp :- Eyebrows :-

Irregular patches of alopecia → giving them the appearance of "moth eaten alopecia"

- Hepatitis , Splenomegaly :-

- generalized Lymphadenopathy.

Cervical, occipital, axillary, epitrochlear.

- Discrete, Rubbery, painless

- Overlying skin = Normal

✱ Skin manifestation :-

1- Skin Rash :- Syphiloderm syphilids



## - Bilateral & Symmetrical Maculopapular Rash

- generalized
- Show variable scaling giving a psoriasiform appearance
- Coppery Red colour.
- Cause: Itching in some pts.
- Occur at anterior Hair line giving rise to (Corona veneris) OR hair line on the neck (collar of Venus)

### - the most common sites:

→ palms → soles → papules surrounded by white Ring

### - Important Clinical Red Flag for diagnosis of Syphilis

- there is Laboratory Red Flag in Diagnosis of syphilis (in neurosyphilis)
- in the undernourished OR Immunocompromised Pts → the papules show central necrosis with pus formation → forming pustules with excessive crusts.  
[Oyster Shell OR rupial Syphilis]

[79]

## 2. Mucous Patches :- <sup>74</sup>

- Start as papules that rapidly ulcerate.
- They appear as greyish white patches gives → sloughs → separate → leaving a serpiginous ulcer [snail track ulcer]
- They affect mainly:-  
Lips, tongue, angle of mouth, nose & larynx → hoarseness

## 3. Condyloma Lata

- the most infective lesion of syphilis
- Occur in moist skin areas:-  
axilla, groin, under Breast, Perianal area.
- appear as large fleshy masses with rounded outline
- They have broad neck (sessile)
- Their surface shows: Necrosis with oozing of fluid that is full of treponema.
- They have to be differentiated from Condyloma acuminata (venereal warts)



- that show skin colour, rough surface
- they are Dry lesions and pedunculated.

## ★ Diagnosis of 2<sup>ry</sup> syphilis:-

### 1- Dark ground microscopy:-

- The fluid is obtained from moist lesions such as Condyloma lata or mucous patches

### 2- Serological tests:-

- They give +ve results in 100% of ptns.

\*- HIV infected syphilitic ptns → abnormal Serologic test results either

- Very High - very Low or - unusual fluctuating titers.

↳ For these ptns:- Skin biopsy : alternative test

## Early Latent Syphilis:

### ◎ Ch. ch by:-

1. Absence of clinical manifestations
2. +ve Serological tests: VDRL  
TPHA

## ◎ Relapses in early Syphilis:

- |   |  |   |
|---|--|---|
| 1. <u>Clinical relapses</u><br>appearance of clinical manif. of 2 <sup>ry</sup> stage | 2. <u>Serological relapses</u><br>- tests show +ve results after being -ve | 3. <u>Transplacental relapses</u><br>- apparently normal mother will have a syphilitic child. |
|---|--|---|

## Late Latent Syphilis

1. This is non-infectious stage that occurs after the 2<sup>nd</sup> yr of infection and persists for years.
2. The ptn is discovered accidentally During performing the tests for blood donation or premarital tests as +ve Serological tests are the only findings.
3. The Danger in this state is Not the infection But the possibility of neurological or CVS complications
4. The following should be done:-  
↳ CSF examination → to exclude neurosyphilis



↳ X-ray and echocardiography :-  
to exclude syphilitic aortitis

↳ Re-examination of ptn with quantitative VDRL  
or RPR at 3, 6 months interval

- They are to be repeated every year for  
3 years if they are still reactive

## Tertiary syphilis

### ★ Pathology :-

↳ 1. Localized form :- (Gumma)

↳ Size :- Few millimeters to many centimeters

↳ Central necrosis surrounded by peripheral  
fibrous tissue.

↳ under microscope :- marked endarteritis  
obliterans (marked than early phase)  
• marked necrosis

(D + local tissue Hypersensitivity)

↳ The cellular infiltrate formed is :-

Plasma cells, lymphocytes, fibroblasts

with absent or scanty organisms

↳ Lymphadenopathy → Found in Early  
phase is Not found in this stage.

↳ Gumma → occur in Covering structures  
as Skin → S.C, Submucous Tissue  
→ occur in Supporting structures  
as Bone - muscle - joints - viscera

↳ 2. Diffuse form :-

↳ Diffuse syphilitic Reaction in the Organ  
as in tongue or testis.

### ★ Clinical Picture

#### 1. Gumma of Skin :-

- appear as single or grouped nodules  
That are Not Symmetrical

- Nodule → Rounded, Red, freely mobile

- heal by :- thin scar or pigmentation  
or may give Ulcer

- Gumma ulcer :- Clean surface, (Wash-leather)  
[8] punched out edges.



## ② Gumma of S.C. tissue

- the lesion later become attached to the overlying skin and gives Ulcer with punched out edges and wash leather floor.
- the ulcer heal with :- thin atrophic non-contractile scar (tissue paper scar)
- the main site are :- Lower leg  
Face - Buttocks

## ③ Gumma of Mucous membrane

- gives :- Ulcer → lead to perforation in the palate → Destruction in nasal septum or laryngeal stenosis
- Syphilis of tongue →
  - occur either in primary stage (chancres)
  - 2<sup>nd</sup> stage (mucous patches)
  - Tertiary stage in 2 forms
    - Localized (Gumma) → ulcerate
    - Diffuse interstitial fibrosis

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leading to → thickening of the tongue and glazed surface (atrophied papillae), fissuring leukoplakia (white thick plaque), S.C.C.

## ④ Gumma of Supporting Structure:

### A Bones:

#### ① Syphilitic periostitis (Long Bone):

- Cellular infiltration of :- plasma cells, lymphocytes, epithelioid cells, giant cells, osteoblasts around the blood vessels

↳ leads to :- stimulation of new bone under the periosteum with rough irregular surface.

- this new bone formation leads to: thickening of the bone. so No pathological fracture.

- it affects mainly: Tibia.

#### ② Syphilitic Osteomyelitis (Flat Bone):

- Cellular infiltration in medullary cavity
- No. sub-periosteal new bone formation
- ↳ This renders Bone Destruction more likely to occur.



- It affects mainly → Skull vault → giving it worm-eaten appearance.

- The hard palate & Nasal septum may be affected.

- Clinically:

- History of trauma followed by → Deeply seated pain (may be very severe) specially at night associated with :- Swelling of the Bone

• Perforation in palate → give rise to Difficult Breathing

- Radiologically :-

- The long Bone show thickening of the periosteum and opacity in medullary cavity. It → new Bone formation

- in the Tibia → apparent on its anterior part giving it a bow-like appearance. (sabre tibia)

- Skull show: Osteoporosis

## B Cartilage :-

• Pericondritis in the ear, nasal septum, Costal cartilage & Destruction.

## C Viscera :-

### Liver

- multiple localized gummata
- with Fibrous Tissue formation
- Distortion of shape of liver without affect its function
- may affected by Diffuse Fibrosis
- ends by: Liver Cirrhosis & disturbed liver function
- portal HTN
- Splenomegaly

### Stomach

- localized or diffuse gummata as reaction
- with dyspepsia similar to peptic ulcer.
- Diagnosed by: Endoscopy & Biopsy

### Testis

- Localized or diffuse Reaction
- Painless enlargement of testis
- Loss of sensation
- gumma may ulcerate Through scrotal skin giving: anterior scrotal ulcer that different from Tuberculous ulcer which found in :- posterior surface of Scrotum & epididymis That is on The post aspect of testis.



# CVS Syphilis

## ★ Pathology :-

- Occur in :- 10-15% of untreated ptns
- after :- 10-15 yrs Common in males.

## A Syphilis of Heart

- ↳ may be Localized (gamma) which may affect the septum → Heart Block
- ↳ may be Diffuse → affect Myocardium leading to → Heart failure.

## B Syphilis of Medium vessels

- ↳ may Destroy the elastic layer of media → aneurysmal Dilation.
- ↳ proliferation of intima → pathological narrowing.
- ↳ it affect
  - ↳ Cerebral vessels
  - ↳ Spinal vessels
  - ↳ Carotid, iliac, femoral arteries

## C Syphilis of Great Vessels (Aorta)

1) ↳ the organism reaches the vessel through Vasa Vasorum in the adventitia → where it excites Cellular infiltration of plasma cells and lymphocytes with late fibrosis in the adventitia and narrow Vasa Vasorum

2) ↳ these changes lead to → fibrosis, Destruction of the media with stretching, aneurysm formation.

↳ Saccular Type.  
(- Aneurysmal Dilation D.t atherosclerosis has fusiform appearance)

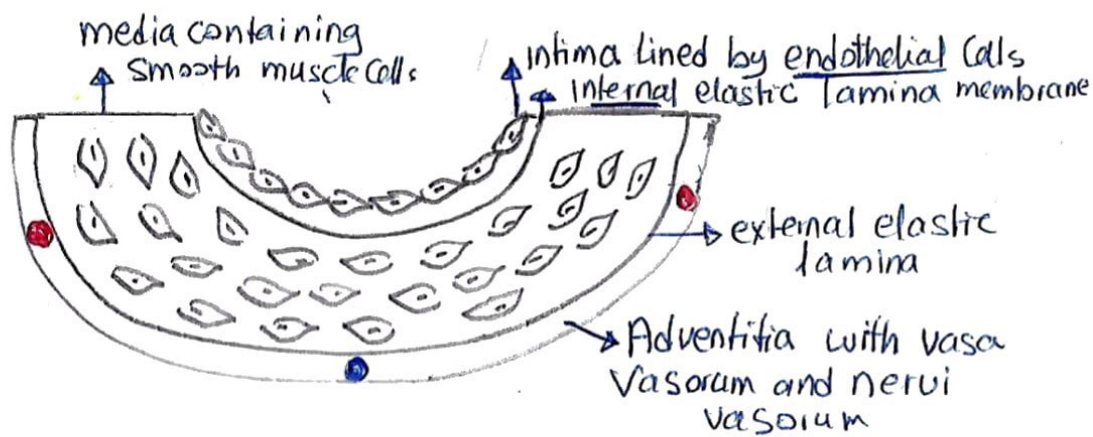
↳ if Dilation → extends into aortic ring → it leads to aortic incompetence

3) ↳ these changes leads to → Distortion

- ↳ thickening
- ↳ Calcification patches on intima

- If extends to their openings at the root of aorta → leads to → Coronary ostial stenosis





## ★ Clinical picture :-

### ① Uncomplicated Aortitis :

- Few symptoms, signs
- lead to → retrosternal Dull aching pain  
Due to stretch of nerves in the sheath of artery

### ② Aortic Regurgitation :-

#### Symptoms

- \$ of left heart failure :-
- Dysnea on exertion or at night → complicated By- Heart failure of Right side with swelling in the abdomen and Lower limbs + upper abd.

Pain → palpitation D.t Hyperdynamic Circulation

#### Signs

- 1- Water hammer pulse :- D.t High systolic pressure and Low Diastolic pressure at Radial artery
- 2- pistol shots :- D.t the same cause (at the femoral artery)
- 3- prominent capillary pulsation at the skin & nail Bed
- 4- Cardiac signs :
  - left ventricle enlargement
  - forcible Apex beat
  - aortic Diastolic murmur over aortic area
  - mid-Diastolic murmur heard over apex.

## ③ Aortic Aneurysm :-

### 1- Ascending aorta :

- most common site
- Its Rupture lead to Sudden Death D.t Cardiac tamponade.
- suspected by presence of parasternal dullness and aortic systolic murmur.

### 2- Arch of the aorta :-

- Pressure on :-

3 tubes	3 nerves	3 vessels	3 Bones
• Trachea ↓ Stridor	• left Recurrent laryngeal nerve ↓ Hoarseness	• Aortic Branch • azygous vein • Sup. vena. Cava.	• Ribs • Sternum • Vertebrae ↓ erosions + fracture
• Oesophagus ↓ Dysphagia	• Phrenic N. ↓ Diaphragmatic paralysis		
• Thoracic Duct ↓ edema of Lower limb	• Sympathetic Chain → Horner \$		

### 3- Descending Aorta

- erosion
- Lower Back pain



## D Coronary Osteal Stenosis :-

- Anginal pain on exertion or at Rest (Angina of Lewis)
- Coronary Thrombosis  $\rightarrow$  Sudden Death

## ★ Diagnosis :

1- Clinical picture

2- X-ray :

- linear Calcification of aorta
- Left Ventricular enlargement
- Aortic aneurysm
- Erosion of ribs, Sternum, Vertebrae

3- ECG :

- Left axis Deviation
- Arrhythmia
- Elevated S-T segment
- T-wave changes

4- Serological tests for syphilis = +ve

# Neurosyphilis

## A Asymptomatic Neurosyphilis :

$\rightarrow$  No neurological manifest, but CSF show changes :-

- Cell Count (Lymphocytes)  $> 5$  HPF
- Protein  $> 40$  mg/l.
- +ve Serological test for syphilis
- Colloidal gold test :-

$\rightarrow$  ratio of albumin to globulin in the CSF may show :- The predominance of globulin that precipitate colloidal gold over albumin that protect it from precipitation

$\rightarrow$  if these findings are present even in absence of symptoms and signs  $\rightarrow$  the pt. may develop :- Symptomatic neurosyphilis [Red flag of Stokes]

## B Meningeal neurosyphilis :

1- Brain :-

★ meninges of the Vertex :

- $\rightarrow$  Convulsions, aphasia, Confusion
- $\rightarrow$  headache, vomiting, papilledema



## ★ Meninges of the Base :-

↳ paralysis of Cranial nerves 3, 4, 6, 7, 8  
leads to Ocular, Facial, Auditory Complications

## ★ Ventricles :-

↳ Hydrocephalus  
↳ subependymal gliosis → Argyl Robertson pupil

pinpoint irregular pupil  
Loss of light Reflex  
preserved accommodation reflex

(Ependyma :- membrane lining the Cerebral Ventricles and the Central canal of spinal cord)

Gliosis :- fibrosis of in the nervous tissue)

## 2- Spinal Cord :-

- The affection of Cervical Region leads to → Lower motor neuron lesion at the level of the Shoulder girdle

Upper motor neuron lesion Below the level of the Cervical region [Erb's Spastic paraplegia]

## [C] Vascular affection :-

- affection of Cerebral - Spinal vessels by [87] →

narrowing or thrombosis → Vascular Ischemia

- may be gliosis of different tissues & different neurologic manifestations :-

↳ Occlusion of ant. spinal artery → paralysis of lower limbs & Urinary incontinence

↳ Occlusion of the post spinal artery → Sensory loss below the level of lesion.

## [D] Parychematous Neurosyphilis :-

### ⊙ Localized affection (gumma)

- rare affection  
- gives → general manifestations of :-  
↑ Intracranial tension → headache  
→ Vomiting  
→ papilledema.  
+ specific manif. according to the involved area.

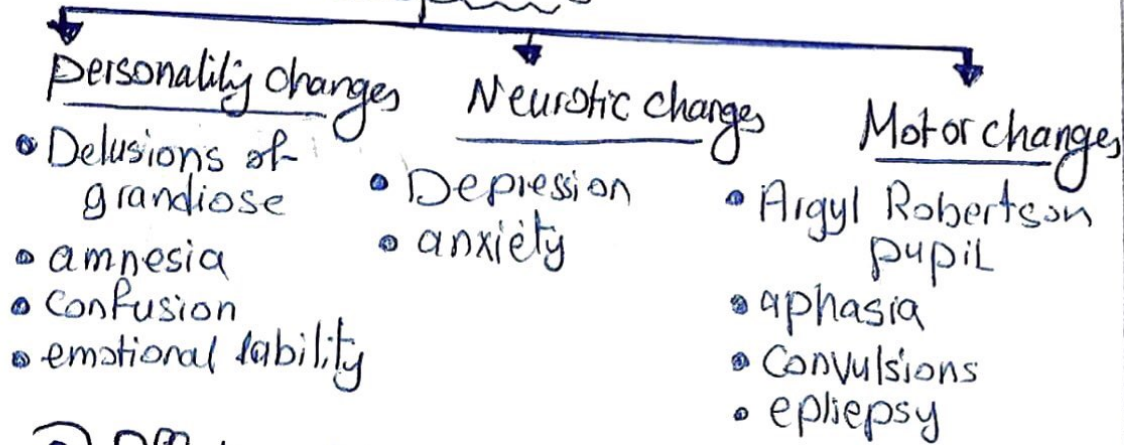
### ⊙ Affection of the Brain

→ lead to :- general paresis of insane  
- Diffuse infiltration of Cerebral Cortex  
→ thickening and adherence of the Dura



to the skull vault and atrophy

- Gliosis of Cerebral cortex with dilated Ventricles → manifested by:



## ① Affection of the Spinal Cord:-

→ leads to:- Tabes Dorsalis  
→ Diffuse infiltration of the spinal cord → degeneration of lumbosacral Region mainly:-  
in posterior roots, post. Column, Posterior ganglia

→ the following manifestations:-

- 1- Progressive loss of vision D.t:- optic nerve atrophy
- 2- Tabetic Crisis:- there is sudden attacks of acute abdomen, renal colic, tenesmus, Laryngeal stenosis → Stridor

3- Urinary - Rectal Troubles as:- 88  
incontinence of urine & stools

4- Sensory ataxia:- D.t → Loss of proprioceptive sensations (sense of position)

5- paresthesia in the Legs

6- Lightening pains:- Intermittent attacks of severe pain in the legs.

7- Trophic changes:- Result from:- Loss of nerve supply.  
manifest by:-

- Skin:- perforating ulcer in sole of foot

- Joints:- Charcot joint → painless  
Hypermobile joint → ends by degenerative changes D.t repeated Trauma.

- affect Knee joint

- Clinically: the joint is   
painless  
Hypermobile  
deformed.

- Radiologically:-

- joints show Erosion - Destruction of Cartilage - osteophytic growths  
- Sclerosis of bony ends.



# Congenital Syphilis

## (A) Introduction:

[A] *T. pallidum* in maternal circulation → pass through placenta after the 4<sup>th</sup> month of pregnancy to the foetal circulation

→ which produce the following effects in the successive pregnancies according to:

[Kassowitz law]

- Abortion after 4<sup>th</sup> month of pregnancy
- Premature baby
- Stillborn baby
- Liveborn baby will develop signs of syphilis
- Liveborn baby will remain healthy.

→ There is Better prognosis with successive pregnancies. It → Prolongation of the period from the Date of the infection of the mother.

[B] Baby may be healthy at Birth But may develop syphilis after weeks or months one should depend on:  
Investigations of the Blood taken from Umbilical vein acc. to Profeta Law:-

→ Blood taken from umbilical vein → give -ve serological tests

But this doesn't exclude syphilis

Because the infant may develop it later on  
So → should be followed up During 3 months

→ Blood taken from Umbilical vein → +ve Result serological test

But this Doesn't mean that Baby is Syphilitic Because it may be Not passive transfer of antibodies from the mother.

[C] More reliable test "Fluorescent treponema absorption" FTA test

using Fluorescein labelled (IgM) that Doesn't cross the placenta → So will Not give False +ve Results

[D] other test: repeated estimated of antibody titre.



# [A] Early Congenital Syphilis:

- Occur in: First 2 yrs
- Clinical manifest: = 2ry syphilis as it's a Blood Born Infection → No 1ry stage.
- The infant → may have the Chancere of the 1ry stage from a recently infected mother During Vaginal Delivery.

• The manifestation include:

## 1- Skin manifest:

- generalized Skin Rash. = Rash of 2ry stage.
- papular, papulosequamous, Macular.
- Differ from stage 2 → it may be a bullous eruption specially on the palms - soles → That rupture to give Large raw Crusted area.
- mucous patches → affect the nasal mucosa giving rise to Syphilitic rhinitis → Difficult suckling
- Condyloma lata → similar to adult 2ry stage

## 2- Eye manifestations:

- Choroid oretinitis → manifest by: Salt and Pepper fundus (on ophthalmoscopic exam)

## 3- CNS system:

- Syphilitic meningitis → bulging Fontanels  
Hydrocephalus ↔ stiffness of the neck  
↔ Convulsions

## 4- CVS system: v. rare

## 5- Respiratory: Pneumonia → may be fatal

## 6- Liver-Spleen:

- Hepatosplenomegaly & liver cell failure
- Generalized lymphadenopathy

## 7- Kidney: → nephrotic syndrome → acute nephritis

## 8- Bone, Cartilage:

- \* First year affection: syphilitic Osteochondritis in which there is inflammation in periosteum and Cartilage of epiphysis → painful Swelling of the epiphysis → limitation and loss of limb movements



- This is known as "Syphilitic pseudoparalysis"

- The Radiological sign is (Characteristic)

↳ Subperiosteal new bone formation → Giving the Bone the onion peel appearance

↳ Loss of density of the upper end of the tibia ~~is~~ "Wimberger Sign"



\* 2nd year affection :

- Syphilitic Dactylitis → Inflammation in the periosteum and Bone of proximal phalanges

↓  
Leads to → painless Pusiform swelling of fingers

● Diagnosis :-

1. Clinical picture
2. Darkground microscopy for discharge of wet skin lesions
3. Radiological picture
4. Serological tests.

## [B] Late Congenital Syphilis

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● Occur :- after the first 2 yrs

● Clinical manifestation :- Tertiary syphilis

● manifests by : Gumma in covering or supporting structure or viscero

● Manifestations [★] Hypersensitivity

1- Interstitial Keratitis :- → most common lesion

- It's a hypersensitivity reaction → Corneal Vascularization + Cellular infiltration

- On slit lamp :- the Vascularization appears Salmon Patches

The infiltrate appear : ground glass.

- The condition Ends by :- Scar, opacity

- The tt → Steroids + antisyphilitic Drugs

2- Cochlear neuritis :-

- It's a Hypersensitivity reaction

- leads to → Inflammation of cochlear nerve + perceptive Deafness



- Conductive deafness → may occur as a complication of syphilitic Rhinitis in the early stage.

### 3- Clutton arthritis

- It's a painless effusion in the joint
- Due to Hypersensitivity Reaction
  - affect mainly → Knee joint with little impairment of mobility.
- The Radiological finding → enlarged joint space • No Bone or Cartilage change.

### ★2★ Bone lesion 2 types of Bone affection

- ↳ First :- new bone formation → gives rise to Parrot's nodes in the skull.
- ↳ Thick medial end of Clavicle → Higoumenakis sign
- ↳ Thick anterior Border of tibia Sabre tibia
- ↳ Second :- → Bone Destruction → Gives Rise to Destruction of nasal septum

with collapse of the lower part of the nose and perforation of palate with food regurgitation

### ★3★ Neurosyphilis

leads to manifestations = a. dults.

### ★4★ CVS - Blood

- CVS affection → v. rare
- Blood affection → Paroxysmal Cold  
 Fever → Haemoglobinuria.  
 rigors → Jaundice • Dark Urine in exposure to cold

Caused by:

- presence of haemolysin that sensitizes the Red Blood cells in the presence of Complement During cold exposure.
- This haemolysin → Disappear on exposure to normal temperature.



# C Stigmata (Remainders) of Congenital Syphilis :-

- permanent scars + Deformation
- Result from → The early lesions of congenital syphilis • Persist for life

## Stigmata of Early lesions

- 1 - Salt & pepper fundus
- 2 - Saddle nose :-
  - Result from → depressed nasal Bridge
  - Dt → Improper Development of nasal septum
- 3 - High arched palate :-
  - Dt Improper development of Maxilla
- 4 - Bulldog face :-
  - Improper development of Maxilla renders the mandible more apparents
  - associated e.g. frontal bossing of the skull and saddle nose make bulldog face.
- 5 - Raghad's :-
  - linear scars at the angles of the mouth.

## Stigmata of Late Lesions

- 1 - Corneal opacity
- 2 - optic atrophy
- 3 - perceptive deafness
- 4 - Frontal bossing of the skull
- 5 - Sabre tibia

## 6 - Hutchinson teeth → Hutchinson triad :-

- upper central incisors are small & widely separated and their sides converge towards the cutting edge → notch
- occur as a result of impaired tooth development

- interstitial Keratitis
- perceptive deafness
- Hutchinson teeth

## 7 - Moon's molars :-

- the first lower molar :- underdeveloped cusps with irregular surface.



# ⊕ Serological tests :-

## ⊙ Non-Specific tests :- of syphilis

- Demonstration of an antigen other than T. pallidum
- This antigen called: **Cardiolipin**  
[alcoholic extract of beef heart muscle]
- It has the ability to React with a gammaglobulin fraction of ptn's Serum called **Reagin**
- This Reagin → present in very small amounts in all normal sera. But in large amounts in the sera of syphilitic ptns to the Degree of reacting with the antigen Cardiolipin
- to produce → Visible Reaction either through → Flocculation OR Complement fixation Reaction.
- The other name of those Tests:-
  - non-treponemal tests
  - Reagin test

## \* the advantages of these tests:-

- Cheap and easy to performed
- good screening tests
- They become -ve after the effective the so
- They can be used in Follow up of ptns under treatment specially if quantitative estimation of their titre is performed

## \* the Disadvantages of Tests:-

- give Both False +ve and False -ve results so they have to be Confirmed i.e. one of the specific treponemal test.

## ⊙ False +ve Results: Dueto:-

- 1- technical faults in samples collection or reagents
- 2- Physiological conditions in pregnancy.
- 3- Old age.
- 4- Pathological conditions in which there is liberation of the antigen **Cardiolipin** from Organisms other than the treponema.  
OR from the mitochondria of the cells in Diseases with tissue Destruction



- Examples :- of acute condition that give False +ve Results

- ↳ Viral pneumonia    ↳ malaria
- ↳ Hepatitis            ↳ measles
- ↳ chickenpox        ↳ vaccination
- ↳ Treponemal Diseases other than syphilis

- Examples of Chronic conditions with False +ve Results:-

- ↳ lupus Erythematus    ↳ RA    ↳ anemia
- ↳ leprosy    ↳ malignancy

★ False -ve Results:- Due to

Prozone phenomenon → in which the High concentration of antibodies in the ptn serum may not give the flocculation reaction except after its Dilution to a particular Low Concentration.

- Those Serial Dilutions of ptn serum used to avoid false -ve Results:-

1. Flocculation tests
2. Complement fixation tests

## II Flocculation tests :-

• The Purified Cardiolipin antigen Mixed with small amounts of syphilitic Serum → Causes Flocculation that can be detected By:- the naked eye or microscope.

• Examples of those tests

① ↳ Venereal Disease research Laboratory (VDRL)

② ↳ Rapid plasma Antigen (RPR) :- done by mixing Carbon containing Cardiolipin antigen suspension with ptn Serum on a disposable Test Card with rotation for 8 minutes

- flocculation of Carbon particles Visible to naked eye.

• Both tests are good Screening tests and can be quantitated to assess the Progress of the Disease in follow up

② Complement Fixation test

Wasserman Reaction (WR)



- In this test the Cardiolipin (antigen) is used which in the presence of the (antibody) in the ptn serum will bind the (Complement)

- In the 2nd step an (Indicator System) formed of Sensitized sheep red cells added

- if the ptn is Syphilitic the Complement is Consumed in the first step → preventing haemolysis of Red cells in the 2nd step.

- many Labs Don't use this test as flocculation tests → easier to perform  
→ cheaper  
→ equally efficient

## 1. Specific Tests :-

- Specific as they depends on: Demonstration of treponemal antigen

- So they called Treponemal Tests:

### ★ Advantages:

- accurate in the Diagnosis
- Don't give False Results
- They performed to Confirm the Results of non-specific test

### ★ the Disadvantages:

- expensive
- technically difficult
- they Remain +ve even after the effective antisyphilitic ~~the~~
- they Can't be used in follow-up of ptn.

## 1. Treponema pallidum haemagglutination

- Relatively simple & less expensive Test
- The antigen → is the Sensitized sheep RBCs that are Coated w/ treponemal antigen added to ptn serum in one test tube
- in other test tube :- the non-sensitized sheep RBCs are added to another sample of ptn's serum [considered the **Control tube**]
- Test considered +ve → when there is visible agglutination of RBCs in the first tube  
↓  
Button shaped D.t presence of antibodies in ptn's serum
- The Control Tube → will not show this Agglutination



Because of its simplicity and lack of need for microscopic examination and Lab. facilities

- It's the most widely using test in Developing Countries including Egypt

## 2 Treponema pallidum immobilization

- The Antigen is the virulent Treponema
- Nichol strain obtained from the infected rabbit added to the ptn Serum in the PF Complement
- If ptn is syphilitic → The antibodies in his serum will inhibit the motility of Treponema
- This test is Technically Difficult
- needs microscopic examination.

## 3 Fluorescent Treponema Antibody Test

- The Antigen is :- Suspension of dead Treponema pallidum (Nichol strain) That is placed on the slide together with the ptn serum.

- Syphilitic antibodies if present in the serum → will coat the Treponema

- To test for this union → Fluorescein (labelled antihuman globulin Conjugate) is added.

→ If the syphilitic antibody has coated the Treponema → The Conjugate reacts with them → producing :- fluorescence when viewed under the Ultra-violet microscope

## 4 Fluorescent Treponemal antibody absorption Test

- The ptn's Serum is diluted at first with a Culture extract of other Treponema to absorb the non-specific antibodies of other Treponemas.

- The Rest of the Test → is performed as previous.

- This modification → will avoid false +ve results of the test Due to other Treponema



- The Advantages of this test :-  
↳ The only +ve test in the early phase of try syphilis.

↳ the test can be made more specific by the use of **Specific** class of fluorescein labelled antihuman globulin against human (IgM)

- Since IgM antibodies Can't cross the placenta → a reactive test in the infant specifically indicates: Congenital syphilis infection.

- The frequent determination of the titers using the non-treponemal test in the infant is :-

↳ less expensive  
↳ more easy to be performed

- They are the standard tests in the Diagnosis of Congenital syphilis in infants

## 5 Reiter protien Complement Fixation Test

- The Antigen is :- the protien derived from Reiter strain of treponema that is Antigenically similar to T. pallidum

- Its added to the ptn Serum with a Complement  
- Its Not in common use as other previous tests

## ± Treatment of Syphilis.

### ① → Basic principles :-

1 - The Drug of choice for the treatment of syphilis is penicillin

2 - The treponema → Can reach any Organ in Body including: CNS in 40%.

↳ This Require Antibiotic that passes BBB  
3 - The average doubling time of Treponema is over 30 hrs → which requires a treponemicidal level in the invaded tissue for at least 8 days.

- They are also affected by Low levels of Penicillins in Blood that are (0.03 unit/ml)



4 - Because of CNS  $\rightarrow$  invasion in 40% of ptns and the inability of the Long-acting Benzathine penicillin to pass BBB

The Drug of choice is  $\rightarrow$  Procaine Penicillin daily injection for 10 days

### ② $\Rightarrow$ Treatment of Early Stage :-

one of the following regimens can be used in the early stage within the first 2 yrs of infections:-

1- Procaine penicillin (600,000) units I.M daily for 10 days (total dose 6 million Unit)

2 - Long acting Benzathine penicillin 2.4 million units  $\rightarrow$  I.M in One single injection.

• although this single long-acting Benzathine penicillin is Better than the repeated procaine penicillin injections as regards the ptn Compliance to treatment

• The procaine penicillin is Better used to save about 40% of CNS complications

### ③ $\Rightarrow$ Treatment of Late Stage

one of these Regimens  $\rightarrow$  used in Late stages after 2 yrs of infection:-

1- Procaine penicillin (600,000) Unit - I.M daily for 20 Days (total 12 million units)

2 - Long acting Benzathine penicillin

3 million units I.M  $\rightarrow$  every week for 4 weeks (total 12 million units)

### ④ $\Rightarrow$ Treatment of CVS Syphilis

= the same of late stage is used in addition to specific ~~tte~~ of Heart failure or aneurysm

### ⑤ $\Rightarrow$ Treatment of Neurosyphilis :-

• The Long acting penicillin  $\rightarrow$  Not effective in this condition as its Lipid insoluble + Have Very Low penetration of BBB

• The Following Regimen  $\rightarrow$  Can used in Order to achieve Treponemicidal levels in the CSF :-